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10/023,427	12/12/2001	Harshal P. Bhagwatwar	U 013528-7	2278

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EXAMINER
FUBARA, BLESSING M

ART UNIT	PAPER NUMBER
1618	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/023,427	BHAGWATWAR ET AL.	
	Examiner	Art Unit	
	Blessing M. Fubara	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *72-90,93 and 96-102* is/are pending in the application.

4a) Of the above claim(s) *100-102* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *72-90,93 and 96-99* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/21/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Examiner acknowledges receipt of request for continued examination under 37 CFR 1.114, amendment and remarks filed 3/16/07. Claims 72, 75, 78, 80, 82-84, 96 and 97 are amended; claims 91, 92 and 94 are canceled. New claims 98-102 are added. Therefore, claims 72-90, 93 and 96-102 are pending.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/16/07 has been entered.

Response to Arguments

Previous rejections that are not reiterated herein are withdrawn.

Election/Restrictions

2. Newly submitted claims 100-102 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: The process for using

the product as claimed can be practiced with another materially different product. For example, radiation therapy is used to treat prostate cancer (claim 13 of US 6,858,598) and breast cancer (A detailed baseline audit of radiotherapy for primary breast cancer: Old habits, new principles *Clinical Oncology, Volume 10, Issue 2, 1998, Pages 95-102, I.C.M. Paterson).*

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 100-102 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Specification

3. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: Claim 86 recites that the concentration of the surfactant or emulsifier with respect to the polymer and organic solvent is between 5 and 50% w/w. While this recitation is present in original claim 13, the specification does not provide support for limitation of between 5 and 50% w/w. Specifically, the specification at paragraph [0062] of the published application supports "weight percentage of the emulsifier with respect to the polymer solution is between 5 and 50%," which is the discontinuous phase The specification at paragraph [0063] supports a situation where the emulsifiers is at 0.001-70% w/w with respect to the oil phase and "more preferably the concentrations are in the range 0.01-50% w/w with respect to the continuous oil phase." Therefore, in light of these citations, the specification does not provide proper support

for the limitation in claim 86. Clarification is required, pointing to the specification for support of the limitation.

Claim Rejections - 35 USC § 112/New Matter

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

6. Claims 72-90, 93 and 96-99 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is new matter rejection.

The requirement by the amended claims presented with the filing of the RCE that the delivery system or product or composition be free of aqueous medium/phase is not supported by the as filed specification. The compositions recited in generic claims 72 and 99 introduce new matter into the claims.

Applicant may overcome this rejection by deleting the new matter from the claims.

7. Claims 72-90, 93 and 96-99 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation that the drug delivery system contains "non-preformed microparticles" is unclear, because the device contains microparticles or it does not. The claims do not say that the "non-preformed microparticles" are microparticle precursors and there is no definition of what the "non-preformed microparticles" could be. If the microparticles are not formed or non-formed before the application of the composition to the target site, it means that the composition does not contain microparticles and there is not any microparticles that are "non-preformed microparticles" in the composition/system.

The rejection can be overcome by correcting the ambiguity in the claims. While paragraph [0154] states that lactic acid has an "anti-ageing effect," lactic acid is also defined in the specification at paragraphs [0078] as "biologically inactive agent" so that the recitation in claim 83that lactic acid is a biologically active agent is ambiguous and confusing because it confusing as to why the lactic acid is a biologically active agent and at the same time a biologically inactive agent.

Clarification is respectfully requested.

Claim 93 requires the composition of claim 72 to further contain biological agent and it is not clear how the composition or delivery system that already contains biologically active agent further contains biologically active agent.

Clarification is respectfully requested.

Claim 78 requires that the discontinuous phase in claim 72 contain water and it is confusing how the claimed delivery system of claim 72, which is free of water or aqueous phase now contains water or aqueous in the dependent claim 78. Claim 78 as presented contradicts the concept of the claimed delivery system of claim 72.

Claim 97 is requires an aqueous medium and it is confusing how the claimed delivery system of claim 72, which is free of water or aqueous phase now contains water or aqueous in the dependent claim 97. Claim 97 as presented contradicts the concept of the claimed delivery system of claim 72.

Clarification is respectfully requested.

8. Claims 85 and 86 recite the limitation "the concentration" in lines 1 and 2. There is insufficient antecedent basis for this limitation in the claim. Claim 72, 76 and 80 do not recite concentration and does not therefore support the claiming of "the concentration" in claims 85 and 86.

9. Claims 88 and 89 recite the limitation "the size of the microparticles" in lines 1 and 2. There is insufficient antecedent basis for this limitation in the claim. Claim 72 and 87 do provide antecedence for "the size of the microparticles" and does not therefore support the claiming of "the size of microparticles" in claims 85 and 86.

10. Claim 96 recites the limitation "the primary mechanism of release" and "the therapeutic agent" (claim 96) in lines 1 and 2. There is insufficient antecedent basis for this limitation in the claim. Claim 72 does not recite primary mechanism or therapeutic agent and does not therefore support the claiming of "the primary mechanism of release" and "the therapeutic agent."

11. Claim 97 recites the limitation "the secondary mechanism of release" and "the therapeutic agent" (claim 96) in lines 1 and 2. There is insufficient antecedent basis for this limitation in the claim. Claim 72 does not recite secondary mechanism or therapeutic agent and does not therefore support the claiming of "the secondary mechanism of release" and "the therapeutic agent."

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

13. Claims 72-79, 84, 87, 93 and 96-99 are rejected under 35 U.S.C. 102(b) as being anticipated by Jain ("controlled drug delivery from a novel injectable in situ formed biodegradable PLGA mocrosphere system," Dissertation, University of Rhode Island, 1998, abstract, cited in applicant's specification).

Jain describes a delivery system that comprises polymer is organic solvent, polymer and emulsifier/surfactant in oil and drug; PEG meeting claim 76 is present; TWEEN meeting the requirements for surfactant/emulsifier in claims 72 and 98 is present (see abstract). Claims 77-79 is product by process claim and reads on the product of Jain. The in situ microparticle forming composition of Jain meets claim 84. The shape of the microparticles recited in claim 87 is inherent to the microparticles formed from the composition of Jain since the microparticles of Jain forms in situ in the same manner as the microparticles are formed in the claimed invention. The biologically active agent of claim 93 is the same as that of claim 72 so that claim 93 reads of the drug of Jain. Jain mixes the phases and the continuous phase further comprises biological agent in the mixture, meeting claim 99. The claims do not state that the agent is present before mixing.

14. Claims 72-79, 84, 87, 93 and 96-99 are rejected under 35 U.S.C. 102(a) as being anticipated by Jain et al. ("Comparison of Various Injectable Protein-Loaded Biodegradable Poly(Lactide-co-glycolide) (PLGA) devices: In situ-Formed Implant Versus In-Situ-Formed Microspheres Versus Isolated Microspheres," in Pharmaceutical Development and Technology, 5(2), 201-207 (2000)).

Jain describes a delivery system that comprises polymer is organic solvent, polymer and emulsifier/surfactant in oil and bovine heart cytochrome c; PEG meeting claim 76 is present; TWEEN meeting the requirements for surfactant/emulsifier in claims 72 and 98 is present (see abstract and pages 201-207). Claims 77-79 is product by process claim and reads on the product of Jain. The in situ microparticle forming composition of Jain meets claim 84. The shape of the microparticles recited in claim 87 is inherent to the microparticles formed from the composition of Jain since the microparticles of Jain forms in situ in the same manner as the microparticles are formed in the claimed invention. The biologically active agent of claim 93 is the same as that of claim 72 so that claim 93 reads of the bovine heart cytochrome c of Jain. Jain mixes the phases and the continuous phase further comprises biological agent in the mixture, meeting claim 99. The claims do not state that the agent is present before mixing.

15. Claims 72-80, 82, 84, 87, 93 and 96-98 are rejected under 35 U.S.C. 102(a) as being anticipated by Jain ("The manufacturing techniques of various drug loaded biodegradable poly(lactide-co-glycolide) (PLGA) devices," in Biomaterials, 21 (2000) 2475-2490).

Jain describes composition comprising drugs such as peptides, vaccines, proteins and micromolecules (abstract); the oil phase I contains PLGA, triacetin (organic solvent for the

PLGA), TWEEN-80, drug, PEG and oil phase II contains miglyol and SPAN 80; the two phases are mixed to form dispersions that upon administration to target site containing water form microspheres in situ (page 2483 and 2484). Claims 77-79 are product by process claims and read on the product of Jain. The in situ microparticle forming composition of Jain meets claim 84. The shape of the microparticles recited in claim 87 is inherent to the microparticles formed from the composition of Jain since the microparticles of Jain forms in situ in the same manner as the microparticles are formed in the claimed invention. The vaccine of Jain meets claim 82. The biologically active agent of claim 93 is the same as that of claim 72 so that claim 93 reads of the drugs/vaccines/peptides/protein of Jain. The oily phase II containing miglyol 812, which is oil and Span 80, which is an emulsifier or surfactant is the continuous hydrophobic phase and the Span 80 is a sorbitan ester meeting claim 80. Jain mixes the phases and the continuous phase further comprises biological agent in the mixture, meeting claim 99. The claims do not state that the agent is present before mixing.

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

17. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

18. Claims 81 and 85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jain ("The manufacturing techniques of various drug loaded biodegradable poly(lactide-co-g;ycolide) (PLGA) devices," in Biomaterials, 21 (2000) 2475-2490).

Jain is described above. Jain uses Span 80, a sorbitan monooleate is a sorbitan ester. Regarding claim 81, which limits the sorbitan ester to sorbitan monopalmitate and sorbitan monostearate, it is known that sorbitan monooleate is a sorbitan ester just as the claimed sorbitan monopalmitate and sorbitan monostearate and one sorbitan ester can be used in place of the other with the expectation of obtaining the same degree of emulsification of the oily phase.

The difference between the prior art and claim 85 is in the concentration of the polymer in the organic phase. The concentration of the polymer in the organic solvent is at a broad concentration of between 1 and 90% so that an artisan is able to use appropriate amount of the polymer in the organic solvent that would provide desired release of the drug. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare the delivery system of Jain with using a concentration of polymer in the organic solvent that would provide the desired release.

19. Claim 86 is rejected under 35 U.S.C. 103(a) as being unpatentable over Jain ("The manufacturing techniques of various drug loaded biodegradable poly(lactide-co-g;ycolide) (PLGA) devices," in Biomaterials, 21 (2000) 2475-2490).

Jain is described above. The difference between the prior art and claim 86 is in the concentration of the emulsifier with respect to the polymer and the organic solvent. The concentration of the emulsifier relative to the organic solvent and the polymer is at a broad concentration of between 5 and 50% so that an artisan is able to use appropriate amount of the emulsifier in the organic solvent and the polymer that would provide desired emulsification of the oily phases. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare the delivery system of Jain with using a concentration of emulsifiers relative to the organic solvent and the polymer that would provide the desired emulsification of the phases.

20. Claims 88-90 are rejected under 35 U.S.C. 102(a) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Jain ("The manufacturing techniques of various drug loaded biodegradable poly(lactide-co-g;ycolide) (PLGA) devices," in Biomaterials, 21 (2000) 2475-2490).

Jain is described above. The difference between Jain and claims 88-90 is the Jain, while disclosing formation of microparticles upon contact of the oily composition with water, does not specifically disclose the particle sizes. However, since the particles are formed by the same process and from the same composition, it would flow that the particles would have the same particle distribution. However, in the alternate, the particles size or the Jain reference would obviously fall within the claimed particle sizes since the particles formed in the claims and the prior art are formed from the same composition and the same process of contacting the composition with an aqueous environment.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Blessing M. Fubara whose telephone number is (571) 272-0594. The examiner can normally be reached on 7 a.m. to 5:30 p.m. (Monday to Thursday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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